PUBLIC SUMMARY DOCUMENT

Product: Pegfilgrastim, injection, 6 mg in 0.6 mL single use pre-filled syringe, Neulasta®

Sponsor: Amgen Australia Pty Ltd

Date of PBAC Consideration: July 2007

1. Purpose of Application

The submission requested an extension to the current section 100 (Highly Specialised Drug) listing for pegfilgrastim to include the primary prophylaxis of chemotherapy induced neutropenia in patients with low-grade Non-Hodgkin's lymphoma (NHL) receiving an anthracycline containing regimen.

Highly Specialised Drugs are medicines for the treatment of chronic conditions, which, because of their clinical use or other special features, are restricted to supply to public and private hospitals having access to appropriate specialist facilities.

2. Background

Both filgrastim and pegfilgrastim are currently only PBS-subsidised for intermediate or high grade lymphoma in patients being treated with aggressive chemotherapy with the intention of achieving a cure or substantial remission.

3. Registration Status

Pegfilgrastim (Neulasta 6 mg in 0.6 mL single dose syringe) was TGA registered on 2 August 2006 for the treatment of patients with cancer following chemotherapy, to decrease the duration of severe neutropenia and so reduce the incidence of infection, as manifested by febrile neutropenia.

4. Listing Requested and PBAC's View

Section 100 (Highly Specialised Drug) Private hospital authority required

Patients being treated with aggressive chemotherapy with the intention of achieving a cure or substantial remission:

Non-Hodgkin's lymphoma (intermediate or high grade; low grade receiving an anthracycline-containing regimen)

Refer to Recommendation and Reasons for PBAC's view.

5. Clinical Place for the Proposed Therapy

Aggressive chemotherapy with an anthracycline containing regimen, is now used across the spectrum of Non-Hodgkin's lymphoma (NHL), and consequently all NHL patients are at similar risk of chemotherapy induced neutropenia. The addition of pegfilgrastim for low grade NHL to the current section 100 listing will enable all patients with NHL treated with an anthracycline-containing regimen to access PBS-subsidised pegfilgrastim to reduce the risk of chemotherapy induced neutropenia.

6. Comparator

The PBAC accepted that the appropriate comparator was no prophylaxis as pegfilgrastim is not available on the PBS for secondary prophylaxis in this setting.

7. Clinical Trials

The submission presented an open-label randomised controlled trial comparing primary prophylaxis (pegfilgrastim used in all patients from the first cycle) with secondary prophylaxis (no pegfilgrastim in the first cycle but used from the second cycle at the discretion of clinicians) among patients with NHL treated with an anthracycline-containing chemotherapy regimen over 6 months

This trial had been published at the time of submission as follows:

Trial/First Author	Protocol title/Publication Title	Publication Citation
Balducci	A Randomized, Open Label, Multicenter Study of Primary Prophylaxis with Neulasta® (pegfilgrastim) Versus Secondary Prophylaxis as an Adjunct to Chemotherapy in Elderly Subjects (≥65 y.o.) with Cancer	Posters presented at ASCO 2005, Chicago Supportive Care 2005, ACCP 2005, and ACCE 2005.

8. Results of Trials

Comparative effectiveness

Across all cycles of chemotherapy, 37.0% of patients in the secondary prophylaxis group experienced febrile neutropenia (FN) whereas 15.1% did in the primary prophylaxis group. The relative risk reduction of 59.3% (33.9%, 84.6%) across all cycles was statistically significant (p = 0.0043), and likely to be clinically important.

The PBAC considered that the sponsor had appropriately extrapolated the results of the trial to patients < 65 years of age.

***Comparative toxicity*:**

The most commonly reported adverse events were neutropenia, fatigue, anaemia and nausea. The most frequently reported adverse event related to pegfilgrastim was bone pain, generally reported to be of mild to moderate severity.

9. Clinical Claim

The submission described primary prophylaxis with pegfilgrastim for patients with low grade NHL as having significant advantages in effectiveness over no prophylaxis and having similar toxicity to its comparators. The PBAC accepted this claim, noting that the extent of treatment effect of pegfilgrastim in reducing the rate of febrile neutropenia was considered to be related to the baseline risk of febrile neutropenia and, in non-Hodgkin's lymphoma, this is related to the intensity of the chemotherapy and not the grade of lymphoma.

10. Economic Analysis

The submission presented a trial-based economic evaluation, limited to consideration of one cycle of chemotherapy, i.e. no pegfilgrastim. The choice of the cost-effectiveness approach was considered valid. The results were expressed as cost per febrile neutropenia event avoided. The resources included were drug costs, and costs of hospitalisation for febrile neutropenia.

The trial-based incremental cost per extra febrile neutropenia event avoided was estimated to be less than $15,000.

The submission also presented a modelled economic evaluation. The choice of the cost-effectiveness approach was considered valid. The trial-based model was extrapolated to the average total number of cycles given and adjusted for age to match the requested population. The outcome was again presented as febrile neutropenia events avoided. The resources included were drug costs and costs of hospitalisation for febrile neutropenia.

The base case modelled incremental cost per extra febrile neutropenia event avoided was estimated to be in the range $15,000 - $45,000.

The PBAC agreed that the base case modelled incremental discounted cost per extra febrile neutropenia event avoided represented acceptable cost-effectiveness and was consistent with previous recommendations for filgrastim/pegfilgrastim.

11. Estimated PBS Usage and Financial Implications

The likely number of packs per year was estimated by the submission to be less than 10,000 in Year 5.

The financial cost per year to the PBS was estimated by the submission to be less than $10 million in Year 5.

12. Recommendation and Reasons

The PBAC recommended extension of the Section 100 (Highly Specialised Drug) listing for pegfilgrastim to include the treatment of patients with low grade non-Hodgkin's lymphoma receiving an anthracycline. This recommendation was made on a cost-effectiveness basis over the comparator, no prophylaxis.

Recommendation:

PEGFILGRASTIM, injection 6 mg in 0.6 mL single use prefilled syringe, Neulasta®, Amgen Australia Pty Ltd

Add to the current restriction:

(Highly Specialised Drug) Private hospital authority required
A patient being treated with aggressive chemotherapy with the intention of achieving a cure or substantial remission in:
Low grade Non-Hodgkin's lymphoma receiving an anthracycline-containing regimen;

Pack: 1

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

Amgen is pleased that Neulasta (pegfilgrastim) will be PBS listed in this patient population with high clinical need and thanks the PBAC for this recommendation.